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Supplementary appendix

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The cost-effectiveness of banning highly hazardous pesticides to prevent suicides due to pesticide self-ingestion across 14 countries: an economic modelling study

Supplementary Appendix

Section 1 – Background and rationale for the analytic approach

Overview

The following section outlines the research context informing the economic evaluation of regulatory bans of highly hazardous pesticides to reduce suicide. It provides a brief synopsis of WHO-CHOICE methods, alongside the background and rationale for various analytic choices implemented in the economic evaluation. These have all been discussed in further detail elsewhere.[1-3]

Research context

The current study was part of an overarching body of work carried out by the WHO Secretariat to develop a menu of policy options and cost-effective interventions for mental health.[1] Provided at the request of WHO Member States, the purpose of this menu is to assist Member States in implementing, as appropriate for national context, actions to achieve voluntary global targets for mental health through the objectives of the Mental Health Action Plan 2013-2020.[4] The list of interventions within this menu is not exhaustive and is intended to provide information and guidance on costs, effectiveness and cost-effectiveness of population-based and individual interventions based on current evidence; and to act as the basis for future work to develop and expand the evidence base. The menu has been developed in line with Appendix 3 of the WHO's Global Action Plan for the Prevention and Control of Noncommunicable Diseases (NCDs) 2013-2020; which uses WHO-CHOICE methodology to prepare and update, as appropriate, estimates on the cost-effectiveness of a range of interventions.[2] This included a new population-based economic analysis for regulatory bans of highly hazardous pesticides to reduce suicide.

WHO-CHOICE methods

Value for money and efficiency are fundamental considerations guiding investment in health, and WHO-CHOICE provides a way to measure them. Cost-effectiveness analysis supports priority setting by defining areas of action where the greatest health gains can be achieved. The use of cost-effectiveness analysis within decision making processes in health is increasingly common globally. However, a series of methodological shortcomings may limit the practical application of cost-effectiveness analysis results. Two examples of this are: methodological differences between studies that limit comparability; and use of the current practice as a comparator, which implicitly assumes current resource use is efficient.

Generalized Cost-Effectiveness Analysis (GCEA) was developed to overcome such shortcomings of traditional cost-effectiveness analysis.[5] The GCEA approach enables both existing and new interventions to be evaluated simultaneously. The comparator used in GCEA is a hypothetical 'null' scenario, where the impacts of all currently implemented interventions are removed. This method uniquely allows existing and new interventions to be analysed simultaneously. Using WHO-CHOICE, the analyst is no longer constrained by what is already being done, and policymakers can revisit and revise past choices if necessary and feasible. They will have a rational basis for deciding to reallocate resources between interventions to achieve social objectives. GCEA also allows the definition of an optimal set of interventions, considering setting-specific factors such as the burden of disease, health system practice and economic conditions.

WHO-CHOICE takes the costing perspective of "the health system", by which is meant the ensemble of actions and actors whose primary intent is to improve human health.[6] WHO-CHOICE therefore includes all direct, market-valued costs, whether public or private, that are required to deliver the intervention, regardless of payer. WHO-CHOICE does not account for non-monetary patient contributions such as travel time, time off work or lost income. It also does not account for costs outside of the health system, such as the cost of social services whose aim is not primarily health oriented. So the costing perspective of WHO-CHOICE is broader than the health sector per se, and is health system focused according to accepted international definitions of the health system. Other sector costs (e.g., legislation) are included to the extent that they are a direct component of the intervention that is intended to improve human health.

In addition to the health system perspective, WHO-CHOICE:

- Uses a standardised method for cost-effectiveness analysis that can be applied to all interventions in different settings;
- Evaluates all interventions relative to the "null", a scenario in which the absence of health care interventions is estimated;
- Uses a population-based approach for estimating health impacts, measured as healthy life years gained (HLYGs) due to an intervention over a 100-year time frame, where one healthy life year gained is equivalent to one disability-adjusted life year (DALY) averted;
- Does not apply discounting to health impacts measured (i.e., HLYGs);
- Uses an ingredients-based economic costing methodology for the calculation of costs. Costs are calculated over a 100-year time frame, discounted at 3% per year and expressed in International dollars (I$) that adjust for the differences in purchasing power between countries; and
- Expresses intervention cost-effectiveness as a ratio of international dollars (I$) per healthy life year gained.

Country income groups

Economic parameters have been assessed for two country income groups: low- and lower middle-income countries (LLMICs); and upper middle- and high-income countries (UMHICs). Recognising the need for generalisability, applicability and comprehensiveness, countries were selected so that a significant proportion of the total population and health burden would be represented. The importance of representation from countries in different regional settings was also recognised. Twenty countries were included in the analysis and are listed below (these are the same countries as for WHO-CHOICE analyses underpinning Appendix 3 to the Global Action Plan for the Prevention and Control of NCDs 2013-2020).[2] Ten countries were analysed from low and lower-middle income settings, and ten from upper-middle and high-income settings. Combined, they represent 63% of the total population, and 65% of the global burden of disease. All economic analyses were first conducted at the country level. Country-specific results were then aggregated to produce corresponding results for the two country income groups.

Low- to Lower Middle-Income countries (LLMICs)	**Upper Middle- to High-Income Countries (UMHICs)**
Bangladesh	China
Ethiopia	Germany
Guatemala	Iran (Islamic Republic of)
India	Japan
Indonesia	Mexico
Nigeria	Russian Federation
Pakistan	South Africa
Philippines	Thailand
Ukraine	Turkey
Vietnam	United States of America

International expert panel

The WHO Secretariat convened a technical consultation in Geneva on 20 August 2019 to review the epidemiologically-based population model, the selected parameters and resulting costs, effectiveness and cost-effectiveness estimates for regulatory bans of highly hazardous pesticides to reduce suicide. International experts were invited by the WHO Secretariat based on their ability to contribute technical advice to the modelling work and to ensure adequate global representation across the six WHO regions (see Acknowledgements of the main manuscript for the full list of experts). All conflicts of interest were declared and checked prior to the meeting. Technical advice was provided in-person during the meeting and through out-of-session email communications. This review informed the development of revised estimates that were presented in a draft WHO Discussion Paper published online on 2 September 2019.[1]

Section 2 – Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement

Section/item	Item No	Recommendation	Section reported
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	See Title
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	See Abstract
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study.	See Introduction
		Present the study question and its relevance for health policy or practice decisions.	See Introduction
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	See Analytic approach subsection in the Methods
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	See Analytic approach subsection in the Methods
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	See Analytic approach subsection in the Methods
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	See Analytic approach subsection in the Methods
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	See Demographic projections subsection in the Methods
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	See Analytic approach subsection in the Methods
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	See Analytic approach and Health impact modelling subsections in Methods
Measurement of effectiveness	11a	Single study-based estimates: Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	Not applicable
	11b	Synthesis-based estimates: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	See Intervention effect size subsection in the Methods and Section 3 of the Appendix

Section/item	Item No	Recommendation	Section reported
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	Not applicable
Estimating resources and costs	13a	Single study-based economic evaluation: Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Not applicable
	13b	Model-based economic evaluation: Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	See Costing analysis subsection in the Methods and Section 5 of the Appendix
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	See the Analytic approach and Costing analysis subsections in the Methods and Section 5 of the Appendix
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	See the Analytic approach, Demographic projections and Health impact modelling subsections in the Methods
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	See Methods and Sections 1, 2, 3, 4 and 5 of the Appendix
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	See Methods and Sections 3 and 5 of the Appendix. Data that were not listed are in the public domain and can be readily accessed online.
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	See Results and Table 2 in the main manuscript. Also see Section 5 of the Appendix.
Characterising uncertainty	20a	Single study-based economic evaluation: Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	Not applicable

Section/item	Item No	Recommendation	Section reported
	20b	Model-based economic evaluation: Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	See Results, Table 2 and Table 3 in the main manuscript. Also see Sections 6, 7 and 8 of the Appendix.
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	See Results. Heterogeneity of results discussed in relation to country income group and the proportion of suicides due to pesticides.
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	See Discussion
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	See Role of the funding source subsection in the Methods
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	See the Declaration of interests

Section 3 – Overview of model parameters

Appendix Table 1 Summary of data used to inform model parameters

	Model parameter	Description
Demographic projections	Population	Data on the 2017 population were obtained by country, age and sex from the OneHealth Tool.[7]
	All-cause mortality	Data on all-cause mortality rates were obtained by country, age and sex from the OneHealth Tool.[7] Data were available by year over the 100-year model time horizon.
	New births	The rate of new births was estimated using country-specific data on the crude birth rate and the sex ratio at birth obtained from WPP 2017.[8] Data were available by year over the 100-year model time horizon.
	Net migration	Country-specific data on the net migration rate were obtained from WPP 2017.[8] Data were available by year over the 100-year model time horizon.
Health impact modelling	Intervention effect size	The intervention effect size was based on a systematic review of international studies examining the impact of national bans on the sale or import of specific pesticides to reduce suicide mortality due to pesticide self-poisoning.[9] This review identified 12 studies that investigated the impact of national bans of specific pesticides across six different countries/territories – Jordan, Sri Lanka, Bangladesh, Crete, South Korea and Chinese Taipei. In Jordan, import bans resulted in 48% fewer pesticide deaths in the three years after the ban compared to the three years prior to the ban.[10] In Sri Lanka, the impact of bans in 2007 led to increasing falls in pesticide suicide deaths across each of the three years following the ban – i.e., by 10% in year one, 28% in year 2 and 41% in year 3.[11] Bans prior to 1998 resulted in an estimated 50% reduction in pesticide suicide deaths between 1995 and 2003.[12-15] In Bangladesh,[16] the ban on all WHO Class I toxicity pesticides led to reductions in pesticide suicides over the following 3 years – i.e., 0% in year 1, 12% in year 2 and 24% in year 3. Reductions continued, following bans on further products in subsequent years. In Crete,[17] there was no statistical evidence of an impact on pesticide suicides over the three years following paraquat bans – but the number of suicide events was very low (i.e., 29 suicides in the three years prior to the ban and 29 suicides in the three years after the ban). In South Korea,[18,19] a ban on paraquat was followed by a 49% fall in pesticide suicides in the year following the ban, compared to the year before. Overall suicide rates were declining at the same time as falls in pesticide suicides. After making adjustments to account for prevailing trends in the overall suicide rate, it was estimated that the paraquat ban led to a 37% decrease in pesticide suicides. In Chinese Taipei,[20,21] pesticide suicide rates declined from 42% of total suicides in 1987 to 12% in 2010. However, the greatest fall in pesticide suicides occurred before most of the bans on WHO Class I toxicity pesticides commenced. In India,[22] a study published after the aforementioned systematic review found that a nationwide ban of endosulfan during 2011 led to the pesticide suicide rate declining by 48% and the overall suicide rate declining by 10%, within three years after the ban. Due to differences in setting, study design and the specific pesticides banned, meta-analysis of these findings was not deemed reasonable. Nevertheless, studies consistently suggested that there were graded annual reductions in pesticide poisoning deaths over three or more years following each ban. Subsequent discussions with an international expert panel, indicated that the intervention effect size should involve a gradual linear

Model parameter	Description
	decrease over 5 years starting from a rate ratio (RR) of 1·00 at baseline to a final RR of 0·65 in year 5. This assumption of a gradual linear decrease was based on trends observed in published studies (see above) and most likely occurs due to the lag between an initial ban and the time it takes to exhaust the available stock of banned pesticides. The effect size estimate of 0.65 was chosen in part based on findings from one of the higher quality studies conducted in South Korea,[18] a country with a track record of collating relatively high quality suicide data.[23] Furthermore, this estimate is a relatively conservative estimate given that greater effect sizes have been reported by some of the studies outlined above. Based on these findings, and subsequent discussions with the international expert panel, it was decided that the intervention effect size would involve a gradual linear increase starting from a rate ratio (RR) of 1·00 at baseline to a final RR of 0·65 in year 5. This gradual linear increase accounted for the lag between an initial ban and the time it takes to exhaust the available stock of banned pesticides. The final RR at year 5 was assumed to be maintained over the remainder of the 100-year model time horizon. These baseline assumptions were deemed conservative as the findings from previous national bans suggest that: a 35% reduction in pesticide suicide rates lies in the mid-range of effect size estimates; and is likely to be maintained indefinitely over time. That is, once a pesticide has been removed from common usage, it is extremely unlikely to be reintroduced later on. The RR will not reduce to zero because HHPs may be substituted by pesticides that are less toxic but are still sometimes lethal. Further bans, as done in Sri Lanka, will likely elicit additional reductions in suicide rates.[14] Intervention effect size estimates are presented in Appendix Table 2. The 95% confidence intervals were determined based on the range of plausible effect size estimates reported by previous studies and were agreed upon by the international expert panel.
Overall suicide rate	The overall suicide rate is equal to the sum of the pesticide suicide rate and the non-pesticide suicide rate. Data on overall suicide rates were obtained for the year 2017 by country, age and sex from GBD 2017.[24] Overall suicide rates occurring between the years 2018 and 2117 were estimated by accounting for historical trends in suicide rates. These trends were based on GBD 2017 data on the average year-on-year percentage change in suicide rates, as observed in each country between the years 1990 and 2017 (see Appendix Table 2).[24] For example, the average year-on-year percentage change in the Indian suicide rate between 1990 and 2017 was -0·46% (SD: 1·98) in males and -1·46% (SD: 2·53) in females. Parametric bootstrapping, using a normal distribution, was performed on the average year-on-year percentage change in suicide rates (calculated above) to estimate the percentage change in suicide rates occurring in each year between 2018 and 2117. For example, using parametric bootstrapping we calculate estimates for the year-on-year change of -2·4% in year one, +2·8% in year two and -1·1% in year three. If the suicide rate for Indian females aged 15 to 19 years was 18·9 deaths per 100,000 during 2017, then the suicide rate would be: 18·4 per 100,000 in year one (18·9 × [1 - 0·024]); 19·0 per 100,000 in year two (18·4 × [1 + 0·028]); and 18·7 per 100,000 in year three (19·0 × [1 - 0·011]).

	Model parameter	Description
	Proportion of suicides due to pesticide self-poisoning	The pesticide suicide rate is equal to the proportion of suicides due to pesticide self-poisoning multiplied by the overall suicide rate. Data on the proportion of suicides due to pesticide self-poisoning were estimated for the year 2017 based on the availability of either: (1) country-specific data from the WHO mortality database;[25] (2) country-specific data from nationally representative surveys;[16,26,27] or (3) WHO regional estimates estimated by a previous meta-analysis, when country-specific data were not available.[28,29] In the uncertainty analysis, proportions with uncertainty ranges denoted by a range (between the smallest and highest values) were modelled using the Pert distribution; with arguments comprising the minimum, middle and maximum values. Conversely, proportions with uncertainty ranges denoted by a sample size (N) were modelled using the beta distribution - i.e., the conjugate prior of the binomial distribution. Proportions occurring between the years 2018 and 2117 were estimated by accounting for declining trends in the percentage of the total working population employed by the agricultural sector (which will reduce pesticide suicide rates over time due to reduced access to HHPs). These trends were based on ILO data on the average year-on-year change in the percentage of total employment involving agriculture; as observed in each country between the years 1991 and 2017 (see Appendix Table 2).[30] It was assumed that the average year-on-year change in the proportion of suicides due to pesticide self-poisoning was perfectly correlated to the year-on-year change in the percentage of total employment involving agriculture. For example, if a country's total employment in agriculture decreased by 3% (from 40% to 37%) in a given year, then the proportion of suicides due to pesticides would likewise decrease by 3% in the same year. Parametric bootstrapping, using a normal distribution, was performed on the average year-on-year change in the percentage of total employment involving agriculture (calculated above) to estimate the percentage change in the proportion of suicides due to pesticides occurring in each year between 2018 and 2117.
	Changes to the non-pesticide suicide rate due to means substitution	The non-pesticide suicide rate is equal to the difference between the overall suicide rate and the pesticide suicide rate. The model accounted for means substitution (i.e., when people attempt suicide using an alternative method after access to HHPs is restricted) by modelling increases in the non-pesticide suicide rate. This was done by assuming that the non-pesticide suicide rate would increase independently of the pesticide suicide rate by a factor of 0·5% per year over the course of 10 years. Overall, this assumption would result in a total increase in the non-pesticide suicide rate of 5% after ten years and is in line with long-term trends observed in Sri Lanka following successive national bans of HHPs.[13,14] Data from Sri Lanka was used as the basis for this assumption as it is the only country which has enacted a ban of HHPs and possesses in-depth data on patterns of suicide due to all other methods over a time horizon of at least 10 years (see Figure 4 of Gunnell et al.[13] where a rise in suicides due to hanging is observed following a ban of all Class I pesticides in 1995). The 0·5% annual increase in the non-pesticide suicide rate was further multiplied by a 'scaling factor' to ensure that the rate of means substitution was directly proportional to the initial proportion of suicides attributable to pesticide self-poisoning. The scaling factor was calculated as the country-specific proportion of suicides due to pesticides divided by 50%. The divisor of 50% was based on the proportion of suicides due to pesticide self-poisoning that was observed in Sri Lanka prior to enacting bans of specific pesticides.[12-15] It follows that countries with a high proportion of suicides due to pesticides will have a proportionately higher increase in the non-pesticide suicide rate due to means substitution and vice versa. For example, the proportion of suicides due to pesticides was 31·5% in India during 2017. The scaling factor would thus be 0·63 (i.e., 31·5% ÷ 50%) and the annual increase in the non-pesticide suicide rate would be 0·315% (i.e., 0·5% × 0·63).

	Model parameter	Description
	Disability-Adjusted Life Years (DALYs)	Intervention health impacts were summarised using the DALY measure, which is the sum of the total Years of Life Lost (YLL) and Years Lived with Disability (YLDs) in the population. The estimation of YLLs and YLDs are described in the following rows.
	Years of Life Lost (YLLs)	YLLs were estimated for each age-sex cohort by: taking the number of all deaths experienced by a cohort in a particular year; and multiplying this by the potential years of life lost. The potential years of life lost were, in turn, calculated as the lowest value of either: the difference between the current age of the cohort and the average life expectancy in the country; or the difference between the current age of the cohort and the remaining time before the end of the 100-year model time horizon. For example, a person dying at age 50 in the baseline year of 2017 would lead to 30 YLLs (if the average life expectancy was 80 years); while a person dying at age 50 in the year 2117 (i.e., the final year over the 100-year time horizon) would only lead to one YLL. Overall, total YLLs in the intervention scenario will be lower than total YLLs in the comparator scenario due to the reduction in suicide mortality due to pesticide self-poisoning. Data on the average life expectancy of males and females in each country were obtained from GBD 2017.[24] YLL estimates were adjusted to account for differing levels of background morbidity experienced by different age groups. For example, YLLs among older individuals (e.g., those aged 65+ years) will be lower as they experience greater background morbidity due to age-related chronic diseases (e.g., cardiovascular disease, cancers, stroke, dementia) when compared to younger individuals. YLLs were adjusted by multiplying each age-specific potential year of life lost by: (1 – pYLD), where pYLD is the age-specific prevalent YLD rate due to all causes of disease (i.e., background morbidity). Data on age-specific pYLD rates due to all causes of disease were obtained from GBD 2017.[24]

	Model parameter	Description
	Years Lived with Disability (YLDs)	YLDs were estimated for each age-sex cohort by: calculating the total number of non-fatal pesticide suicides experienced by a cohort in a particular year; and multiplying this by the duration of ongoing disability attributable to pesticide self-poisoning and the relevant GBD 2017 disability weight. The total number of suicide attempts (non-fatal) was calculated by dividing the total number of pesticide suicide deaths by the case fatality proportion of suicide attempts using HHPs. Based on advice from the international expert panel, the case fatality proportion of suicide attempts using HHPs was estimated to be 10% (range: 5 to 15). The case fatality proportion associated with pesticide self-ingestion will vary from country to country and will be dependent on the most commonly used products for pesticide self-poisoning. For the model, the case fatality proportion was assumed to be 10% across all countries and was based on a previous study investigating the case fatality of pesticide self-ingestion in Sri Lanka.[31] A case fatality proportion of 10% was considered reasonable for a multi-country analysis as it is in keeping with the case fatality observed in other countries where paraquat (a highly fatal pesticide with a case fatality proportion >40%) does not dominate the pattern of pesticide self-poisoning. This was deemed a conservative estimate given that the case fatality will likely be higher than 10% when compared to the case fatality observed across the full range of highly hazardous pesticides. The duration of ongoing disability was assumed to be two times the average length of stay (ALOS) following hospitalisation for non-fatal pesticide self-ingestion. This assumption was based on a study involving 94 patients at a tertiary-level hospital in Bangladesh who reported a duration of ongoing illness following pesticide self-ingestion that was approximately double their ALOS.[32] The ALOS used in the current model was 5·1 days (SE: 0·53). This was calculated based on the weighted average ALOS across eight studies of hospital inpatients for pesticide self-poisoning.[32-39]. Medical professionals within the international expert panel confirmed that the duration of ongoing disability outlined above aligned with their clinical experience of treating pesticide self-poisoning cases in LMICs. Overall, the duration of ongoing disability was estimated to be 10·2 days (SE: 0·53). The GBD 2017 disability weight for acute short-term poisoning was 0·163 (95% CI: 0·109 to 0·227).[24] This disability weight is likely to underestimate the disability due to pesticide self-poisoning as pesticide poisoned patients typically experience higher lengths of stay and have a greater need for ventilation when compared to other types of poisoning (e.g., people self-poisoning with analgesics or psychotropic medication).[39] YLD estimates were adjusted to account for differing levels of background morbidity experienced by different age groups. For example, YLDs among older individuals (e.g., those aged 65+ years) will be higher as they experience greater background morbidity due to age-related chronic diseases (e.g., cardiovascular disease, cancers, stroke, dementia) when compared to younger individuals. Data on prevalent YLD rates due to all causes of disease (i.e., background morbidity) were obtained from GBD 2017.[24] A multiplicative function was used to combine age-specific YLD rates due to acute short-term poisoning with age-specific YLD rates due to other causes of disease.

Appendix Table 2 Values and uncertainty ranges for selected model input parameters

Model input parameter	Value and uncertainty range	Uncertainty distribution	Source
Intervention effect size over time, expressed as a rate ratio (RR)	Baseline: 1·00 Year 1: 0·93 (95% CI: 0·91 - 0·95) Year 2: 0·86 (95% CI: 0·83 - 0·90) Year 3: 0·79 (95% CI: 0·74 - 0·84) Year 4: 0·72 (95% CI: 0·66 - 0·79) Year 5+: 0·65 (95% CI: 0·57 - 0·74)	Lognormal	Gunnell et al.[9]
Average year-on-year percentage change in suicide rates, as observed in each country between the years 1990 and 2017 (Males)	Bangladesh: -2·0% (SD: 2·9%) China: -2·9% (SD: 3·1%) Ethiopia: -2·2% (SD: 1·6%) Guatemala: -2·0% (SD: 8·0%) India: -0·5% (SD: 1·9%) Indonesia: -0·6% (SD: 0·6%) Iran: -0·3% (SD: 1·1%) Mexico: 1·3% (SD: 2·7%) Nigeria: 0·3% (SD: 0·8%) Pakistan: 0·4% (SD: 1·4%) Philippines: -2·8% (SD: 7·0%) South Africa: -1·4% (SD: 4·8%) Thailand: -0·2% (SD: 5·1%) Vietnam: -0·6% (SD: 0·6%)	Normal	Global Burden of Disease Study 2017 [24]
Average year-on-year percentage change in suicide rates, as observed in each country between the years 1990 and 2017 (Females)	Bangladesh: -2·0% (SD: 3·5%) China: -4·9% (SD: 4·3%) Ethiopia: -3·8% (SD: 2·3%) Guatemala: -0·4% (SD: 8·7%) India: -1·4% (SD: 2·5%) Indonesia: -1·7% (SD: 0·9%) Iran: -2·3% (SD: 1·7%) Mexico: 2·3% (SD: 2·5%) Nigeria: -1·4% (SD: 2·2%) Pakistan: 0·2% (SD: 4·3%) Philippines: -2·3% (SD: 5·9%) South Africa: -2·7% (SD: 8·0%) Thailand: -2·3% (SD: 5·3%) Vietnam: -1·6% (SD: 0·5%)	Normal	Global Burden of Disease Study 2017 [24]

Model input parameter	Value and uncertainty range	Uncertainty distribution	Source
Average year-on-year change in percentage of total employment involving agriculture, as observed in each country between the years 1991 and 2017	Bangladesh: -2·0% (SD: 1·9%) China: -2·9% (SD: 1·9%) Ethiopia: -0·6% (SD: 1·0%) Guatemala: -0·8% (SD: 4·9%) India: -1·3% (SD: 0·9%) Indonesia: -2·0% (SD: 4·0%) Iran: -1·2% (SD: 2·4%) Mexico: -2·4% (SD: 4·9%) Nigeria: -1·1% (SD: 1·3%) Pakistan: -0·2% (SD: 1·3%) Philippines: -2·1% (SD: 2·0%) South Africa: -2·5% (SD: 7·8%) Thailand: -2·4% (SD: 4·3%) Vietnam: -2·0% (SD: 2·0%)	Normal	International Labor Organization [30]

Abbreviations: *95% CI - 95% confidence interval; SD - standard deviation.*

Section 4 – Four equations used to calculate post-intervention health impacts

Four equations were derived to calculate post-intervention health impacts using the three input parameters for which there was available data: (1) the overall suicide rate; (2) the proportion of suicides attributable to pesticide self-poisoning; and (3) the intervention effect size for the pesticide suicide rate.

Equation (1) estimates the intervention effect size for the overall suicide rate as a function of the intervention effect size for the pesticide suicide rate:

$$RR_{total} = p_{pesticide-}\, RR_{pesticide} + \left(1 - p_{pesticide-}\right) RR_{other} \quad (1)$$

Where: RR_{total} is the intervention effect size for the overall suicide rate, expressed as a rate ratio; $p_{pesticide-}$ is the pre-intervention proportion of all suicides attributable to pesticide self-poisoning; $RR_{pesticide}$ is the intervention effect size for the pesticide suicide rate; and RR_{other} is the intervention effect size for the non-pesticide suicide rate. If RR_{other} = 1·0 in the equation above, then RR_{total} will represent the intervention effect size for the overall suicide rate that would occur if it were solely dependent on post-intervention reductions in pesticide suicide rates.

The occurrence of means substitution (i.e., when people attempt suicide using an alternative method after access to HHPs is restricted) was accounted for in the intervention scenario by assuming that the non-pesticide suicide rate would increase independently of the pesticide suicide rate by a factor of 0·5% per year over the course of 10 years. This adjustment was implemented by assuming that RR_{other} in Equation (1) was equal to 1·00 at baseline, 1·005 in year one, 1·01 in year two, 1·015 in year three, and so forth. Overall, this assumption would result in a total increase in the pesticide suicide rate of 5% after ten years (i.e., RR_{other} = 1·05 at year ten) and is in line with long-term trends following successive bans of HHPs in Sri Lanka.[13,14] The 0·5% annual increase in the non-pesticide suicide rate was further multiplied by a scaling factor to ensure that the rate of means substitution was directly proportional to the initial proportion of suicides attributable to pesticide self-poisoning (i.e., $p_{pesticide-}$). Additional details on the calculation of the scaling factor are provided in Appendix Table 1.

Equation (2) estimates the overall suicide rate that occurs post-intervention, while Equation (3) estimates the pesticide suicide rate that occurs post-intervention:

$$SR_{total+} = RR_{total}\, SR_{total-} \quad (2)$$

$$SR_{pesticide+} = RR_{pesticide}\left(p_{pesticide-}\, SR_{pesticide-}\right) \quad (3)$$

Where: SR_{total+} is the overall suicide rate at post-intervention; SR_{total-} is the overall suicide rate at pre-intervention; $SR_{pesticide+}$ is the pesticide suicide rate at post-intervention; and $SR_{pesticide-}$ is the pesticide suicide rate at pre-intervention.

Equation (4) estimates the mortality rate that occurs post intervention:

$$MR_{total+} = MR_{total-} + SR_{total-}(RR_{total} - 1) \quad (4)$$

Where: MR_{total+} is the post-intervention mortality rate attributable to all causes of death; and MR_{total-} is the pre-intervention mortality rate attributable to all causes of death.

In summary, the four equations outlined above were applied to each age-sex cohort in the model to estimate the overall suicide rates, pesticide suicide rates and mortality rates that occur post-intervention.

Section 5 – Additional details on the costing analysis

The costing framework and methods developed by the WHO-CHOICE programme were used to estimate the country-specific costs of a national ban of highly hazardous pesticides (HHPs).[3,5] WHO-CHOICE adopts an ingredients approach that multiplies quantities of resources required to implement an intervention by the respective price or unit cost of those resources. Resource needs are split between programme-level costs (such as programme management, training, media and regulation) and patient-level costs incurred at the level of the health care facility. Country-specific intervention costs were estimated using previous NCD costing templates developed and used by WHO for evaluating NCD prevention and control; both in the context of identifying 'best buys' and for subsequent work on global 'price tags', NCD investment cases and updates to Appendix 3 of the WHO NCD Global Action Plan.[40,41]

Previous NCD costing templates were modified to account for the different stages involved with implementing national bans of HHPs. A resource needs matrix was used to identify resource needs for a pesticide ban, consisting of four stages of policy development (planning stage [year 1]; policy development [year 2]; partial implementation [years 3-5]; full implementation [year 6 onwards], and six categories of resource use: human resources; training; meetings; mass media; supplies and equipment; and other resources. The cost of training and meetings was based on the frequency of meetings and workshops within a year, their average duration, the number of national and sub-national participants (plus associated support staff), and the size of the meeting venue.

To derive comparable estimates of resource needs across interventions and countries, resource need estimates were made for the different resource categories for a standardized country of 50 million people (split into 10 provinces of 5 million and 10 districts of 0·5 million persons). These estimates were subsequently adjusted to reflect the actual population size and administrative composition of each country. Unit costs for resource items were taken from the WHO-CHOICE database (www.who.int/choice/costs), which contains country-specific estimates for primary care visits of different durations, salaries, per diem allowances (for training and meetings), media costs and consumable items, including fuel and office supplies. Generation of these estimates was based on an econometric analysis of a multinational dataset, using gross national income per capita (plus other explanatory variables) to predict unit costs in different WHO Member States.[42]

Country-specific costs available through the WHO-CHOICE database were converted to 2017 international dollars (2017 I$) using USD consumer price inflation indices for traded goods (e.g., drugs and consumables) and country-specific GDP price deflators for non-traded goods (e.g., staff wages, inpatient days and outpatient visits).[43] All costs were discounted at a 3% annual rate and modelled with ±20% uncertainty ranges using the PERT distribution.

Section 6 – Additional results for the baseline analysis

Absolute results (per 1 population) are presented in Appendix Table 3, while population standardised results (per 1,000,000 population) are presented in Appendix Table 4.

Appendix Table 3 Absolute results for the baseline analysis (per 1 population)

	Category	CE ratio (I$ per HLYG) [a] *(95% UI)*	Intervention costs (2017 I$) *(95% UI)*	Healthy life years gained [a] *(95% UI)*	YLLs averted *(95% UI)*	YLDs averted *(95% UI)*	Pesticide suicides averted *(95% UI)*
Country income group	LLMICs (n = 9)	$94 (73 to 123)	$19·00M (17·16M to 20·77M)	202,446 (156,681 to 252,503)	202,076 (156,376 to 252,096)	371 (221 to 626)	15,328 (11,840 to 19,174)
	UMHICs (n = 5)	$237 (191 to 303)	$10·58M (9·23M to 11·82M)	44,623 (35,580 to 54,565)	44,525 (35,503 to 54,456)	97 (52 to 171)	4,075 (3,313 to 5,035)
Suicides due to pesticides	2 to 9% (n = 5)	$699 (515 to 940)	$6·15M (5·59M to 6·73M)	8,804 (6,656 to 11,920)	8,791 (6,643 to 11,909)	13 (8 to 21)	550 (406 to 749)
	10 to 19% (n = 3)	$598 (449 to 796)	$3·6M (3·19M to 4·02M)	6,015 (4,545 to 7,587)	6,005 (4,535 to 7,576)	10 (6 to 14)	399 (303 to 505)
	20 to 29% (n = 4)	$213 (168 to 281)	$3·87M (3·44M to 4·26M)	18,188 (13,801 to 22,459)	18,141 (13,755 to 22,416)	47 (29 to 78)	1,933 (1,495 to 2,484)
	>30% (n = 2)	$75 (58 to 99)	$15·94M (13·87M to 18·12M)	213,239 (167,181 to 270,743)	212,838 (166,752 to 270,299)	401 (232 to 678)	16,739 (13,154 to 20,650)

Abbreviations: 95% UI: 95% uncertainty interval; CE - cost-effectiveness; HLYG - healthy life year gained; I$ - international dollars; LLMICs - low- to lower middle-income countries; M - millions; UMHICs - upper middle- to high-income countries; YLDs - years lived with disability; YLLs - years of life lost.

[a] Healthy Life Years Gained (HLYGs) are equivalent to Disability-Adjusted Life Years (DALYs) averted – i.e., the sum of YLLs averted and YLDs averted.

Appendix Table 4 **Population standardised results for the baseline analysis (per 1,000,000 population)**

	Category	CE ratio (I$ per HLYG) [a] *(95% UI)*	Intervention costs (2017 I$) *(95% UI)*	Healthy life years gained [a] *(95% UI)*	YLLs averted *(95% UI)*	YLDs averted *(95% UI)*	Pesticide suicides averted *(95% UI)*
Country income group	LLMICs (n = 9)	$94 (73 to 123)	$7,675 (6,931 to 8,389)	81·77 (63·29 to 101·99)	81·62 (63·16 to 101·83)	0·15 (0·09 to 0·25)	6·2 (4·8 to 7·7)
	UMHICs (n = 5)	$237 (191 to 303)	$6,008 (5,237 to 6,709)	25·33 (20·20 to 30·97)	25·28 (20·15 to 30·91)	0·06 (0·03 to 0·10)	2·3 (1·9 to 2·9)
Suicides due to pesticides	2 to 9% (n = 5)	$699 (515 to 940)	$10,769 (9,787 to 11,776)	15·42 (11·65 to 20·87)	15·39 (11·63 to 20·85)	0·02 (0·01 to 0·04)	1·0 (0·7 to 1·3)
	10 to 19% (n = 3)	$598 (449 to 796)	$8,383 (7,439 to 9,363)	14·02 (10·59 to 17·68)	14·00 (10·57 to 17·66)	0·02 (0·01 to 0·03)	0·9 (0·7 to 1·2)
	20 to 29% (n = 4)	$213 (168 to 281)	$8,224 (7,318 to 9,059)	38·66 (29·33 to 47·73)	38·56 (29·23 to 47·64)	0·10 (0·06 to 0·17)	4·1 (3·2 to 5·3)
	>30% (n = 2)	$75 (58 to 99)	$5,762 (5,012 to 6,550)	77·07 (60·43 to 97·86)	76·93 (60·27 to 97·70)	0·14 (0·08 to 0·25)	6·1 (4·8 to 7·5)

Abbreviations: 95% UI: 95% uncertainty interval; CE - cost-effectiveness; HLYG - healthy life year gained; I$ - international dollars; LLMICs - low- to lower middle-income countries; UMHICs - upper middle- to high-income countries; YLDs - years lived with disability; YLLs - years of life lost.

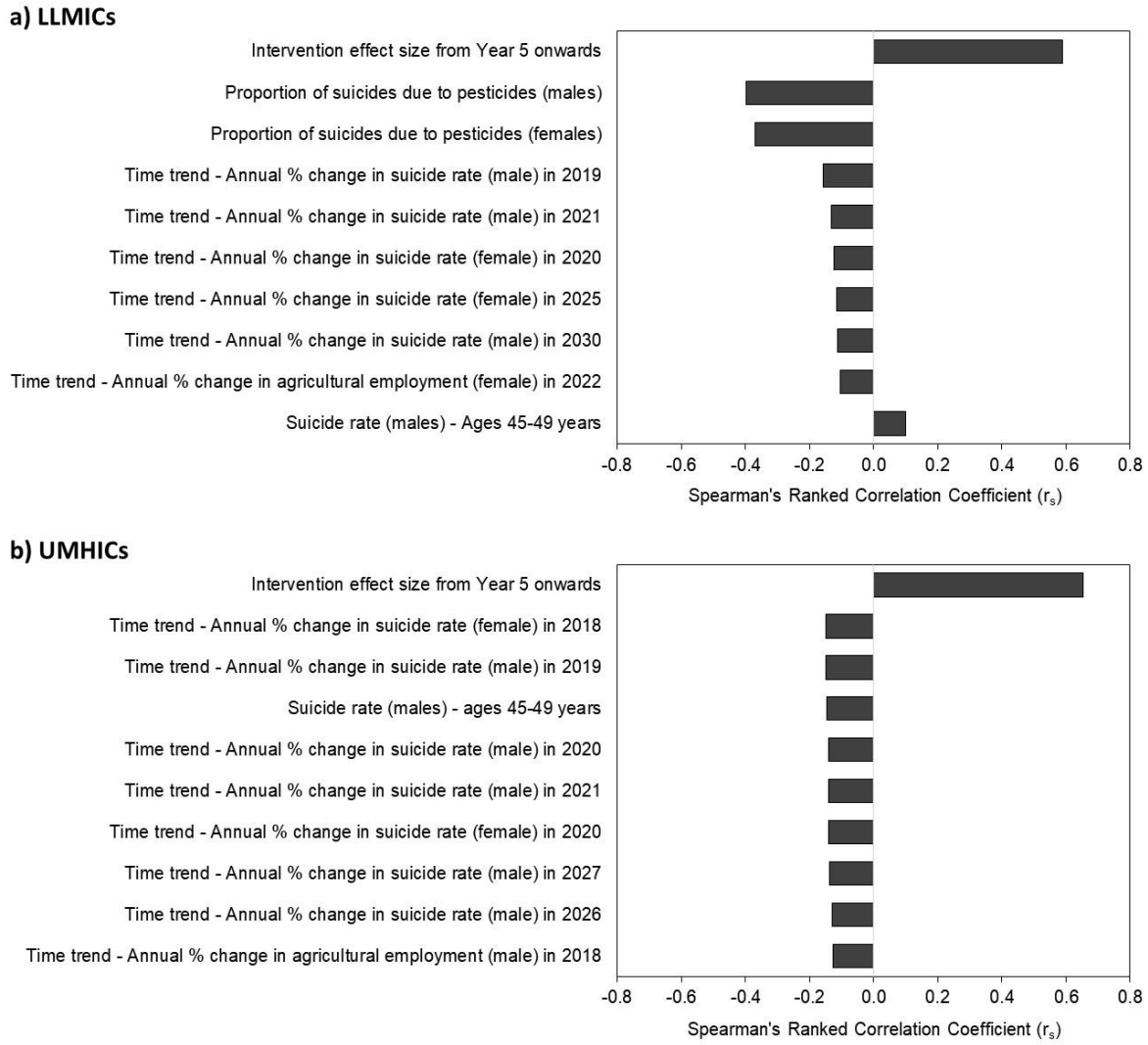
[a] *Healthy Life Years Gained (HLYGs) are equivalent to Disability-Adjusted Life Years (DALYs) averted – i.e., the sum of YLLs averted and YLDs averted.*

[b] *Per 1,000,000 population.*

Section 7 – Multivariate probabilistic sensitivity analysis results

Appendix Figure 1 presents the tornado graphs for the multivariate probabilistic sensitivity analyses conducted among low- to lower middle-income countries (LLMICs) and upper middle- to high-income countries (UMHICs). Each tornado graph outlines the top ten input parameters (out of a total 539) that had the largest impact on the cost-effectiveness ratio. The strength of association between each input parameter and the final outcome was measured using Spearman's ranked correlation coefficient (r_s), where absolute values of: 0.00-0.19 denote a very weak correlation; 0.20-0.39 denote a weak correlation; 0.40-0.59 denote a moderate correlation; 0.60-0.79 denote a strong correlation; and 0.80-1.00 denote a very strong correlation.[44] For LLMICs, the 5-year intervention effect size was moderately correlated with the cost-effectiveness ratio ($|r_s|$=0.59), while the proportion of suicides attributable to pesticides were weakly correlated ($|r_s|$=0.39 for males and $|r_s|$=0.37 for females). The remaining 536 input parameters involved very weak correlations ($|r_s|$<0.20). For UMHICs, the 5-year intervention effect size was strongly correlated with the cost-effectiveness ratio ($|r_s|$=0.65). The remaining 538 input parameters involved very weak correlations ($|r_s|$<0.20).

Appendix Figure 1 Tornado graphs for the multivariate probabilistic sensitivity analyses, presented by country income group

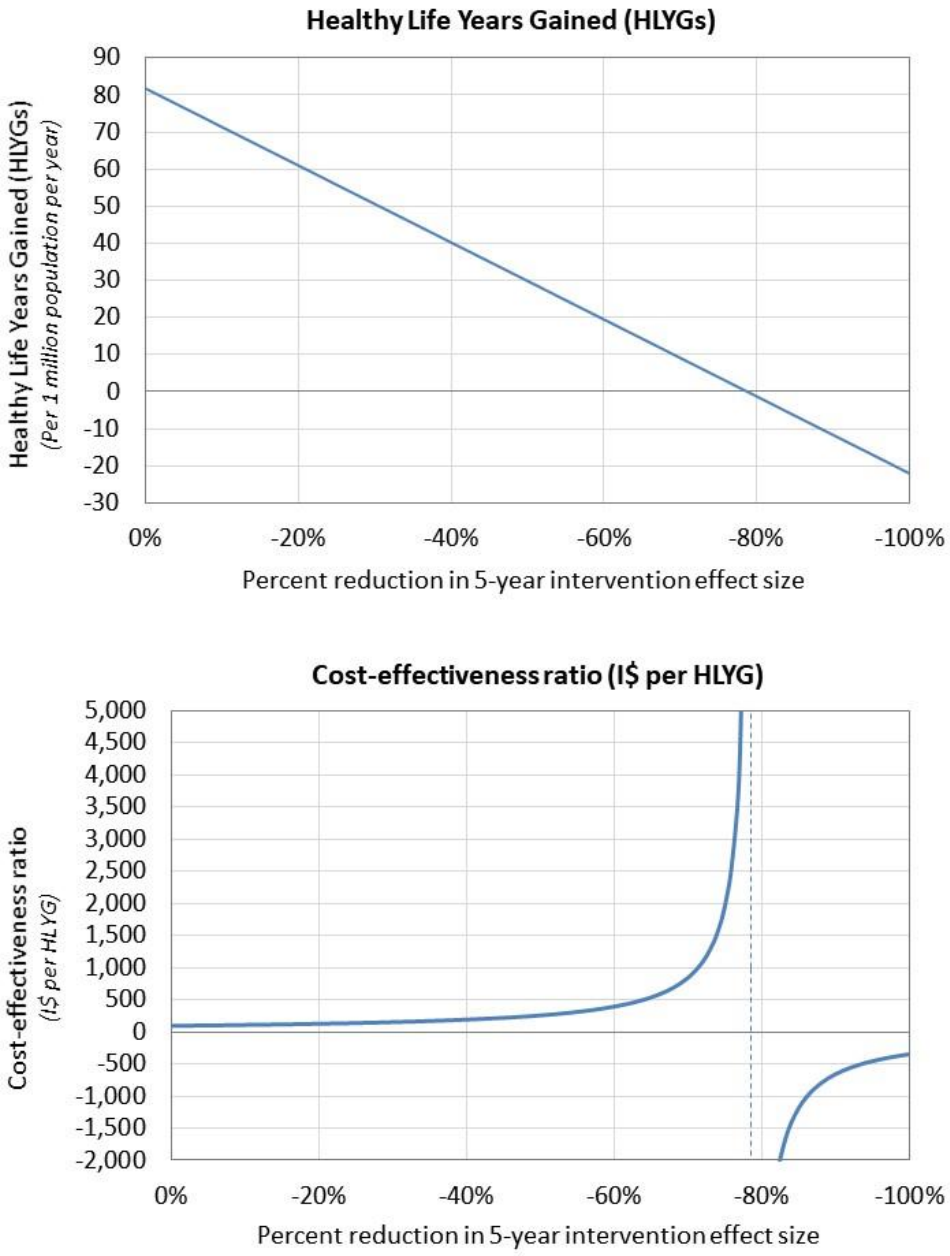


Abbreviations: LLMICs - low- to lower middle-income countries; UMHICs - upper middle- to high-income countries.

Section 8 – Threshold analysis results

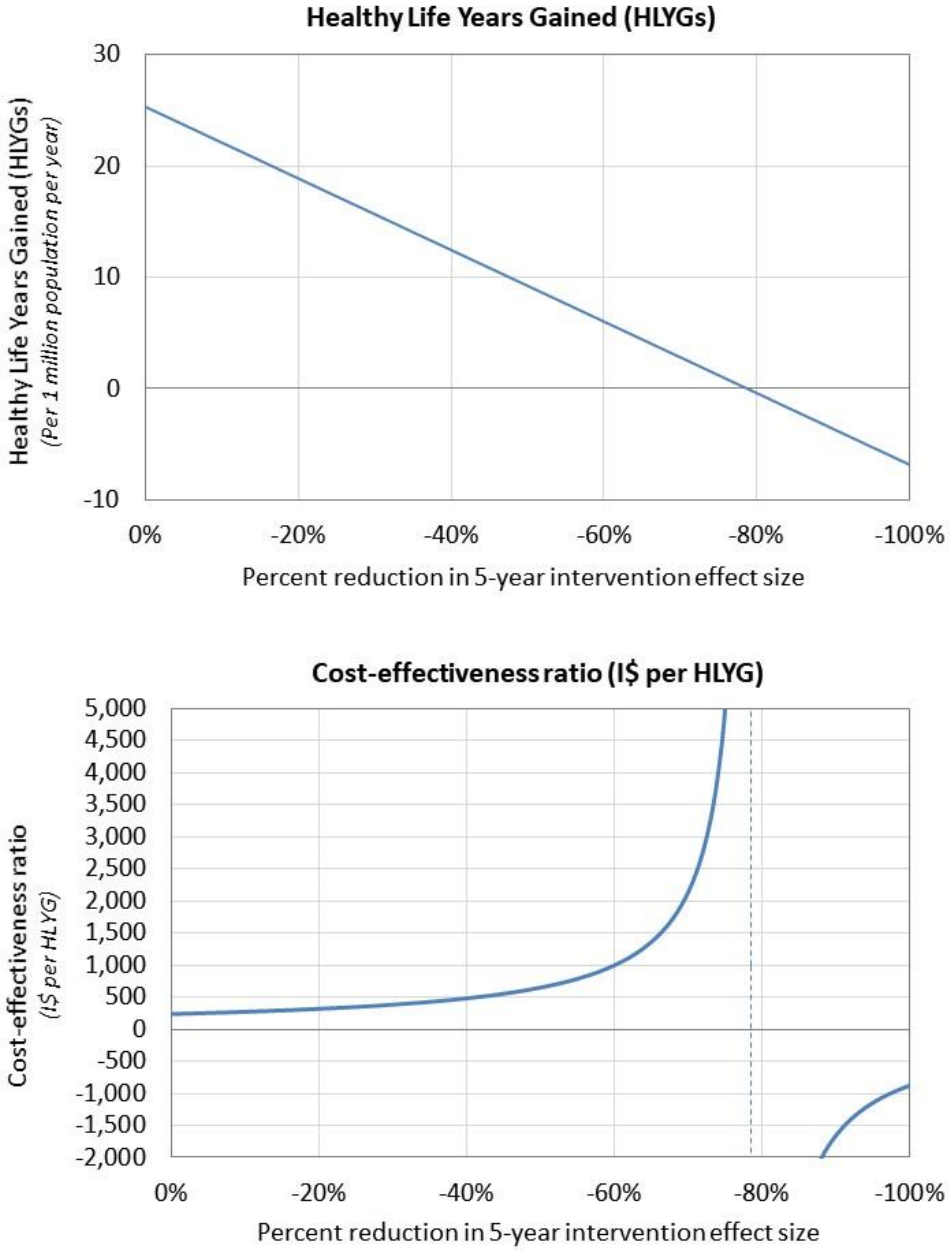
The results of the threshold analysis testing the impact of incrementally reducing the 5-year intervention effect size from 0% (RR=0.65) to 100% (RR=1.00) are presented for low- to lower middle-income countries (LLMICs) in Appendix Figure 2 and for upper middle- and high-income countries (UMHICs)in Appendix Figure 3. Cost-effectiveness ratios remained fairly stable even after large reductions in the 5-year intervention effect size. For example, the cost-effectiveness ratio remained below I$500 per HLYG after a 63% reduction (RR=0.87) among LLMICs and a 41% reduction (RR=0.79) among UMHICs. Across both LLMICs and UMHICs, the intervention became dominated – i.e., incurred higher costs and produced lower health benefits than the comparator – after a 79% reduction (RR=0.93) in the 5-year intervention effect size.

Appendix Figure 2 Threshold analysis results for low- to lower middle-income countries (LLMICs)



Abbreviations: I$ per HLYG - international dollars per healthy life year gained.

Appendix Figure 3 Threshold analysis results for upper middle- to high-income countries (UMHICs)



Abbreviations: I$ per HLYG - international dollars per healthy life year gained.

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